

--One particular application to which luciferase may be put is in an assay for detection of cellular components such as ATP or enzymes such as adenylate kinase (AK), as described in European Patent Application No. 94904295.6. Such assays are useful in detecting the presence of microorganisms in a particular environment. For these purposes, the presence of cellular components which are the target of the assay in the luciferase reagent will produce levels of "background" noise which will have to be taken account of when interpreting results obtained using these products. This is a particular problem in the adenylate kinase assay, which has a high level of sensitivity.--

Page 3, delete the paragraph spanning lines 9 and 10 and insert the following therefor:

--The applicants have devised a new technique where the problem of contamination of products of recombinant DNA technology by undesired or even harmful products can be minimised.--

Page 5, delete the paragraph spanning lines 14 through 19 and insert the following therefor:

--Therefore, an alternative approach is to clone the adenylate kinase gene into a suitable vector such as Promega plasmid "pALTER-1". Site-directed mutagenesis of the amino acids at positions 87 and 107 for example using PCR based methods will give a gene product which has altered thermolability. Screening of these mutants as described above will indicate which substituent amino acids at these positions give adenylate kinase which is more thermolabile than the native protein.--

Page 5, delete the paragraph spanning line 28 through page 6, line 3 and insert the following therefor:

--Conversely and additionally, the desired polypeptide product may be engineered so that its tolerance to the conditions under which the undesired protein is denatured is increased. For instance, in the case of luciferase enzyme, several thermostable mutants are known in the art and these may be employed in the method of the invention. Alternatively other thermostable mutants or mutants which have increased acid stability etc. can be prepared using similar techniques. In this case, the screening process will select those mutants which have increased tolerance rather than decreased tolerance to the condition being used to denature the undesired polypeptide.--

Page 6, delete the paragraph spanning lines 24-30 and insert the following therefor:

--The invention further provides a method for producing a recombinant cell according to the present invention which method comprises in any order (a) transforming a host cell with a vector which encodes said undesired protein in a form which is unstable under given conditions, subjecting transformants to said conditions and detecting those in which protein product is denatured, and (b) transforming said host cell with a vector which encodes a desired polypeptide which is stable under said conditions and a first selection marker, and using the first selection marker to detect stable transformants.--

Page 7, delete the paragraph spanning lines 15-22 and insert the following therefor: